DEPARTMENT OF HEALTH & HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

PHILADELPHIA DISTRICT
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Philadelphia, PA 19106

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WARNING LETTER
05-PHI-03

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

February 24, 2005

Katherine D. Crothall, PhD, President/Chief Executive Officer
Animas Corporation
200 Lawrence Drive
West Chester, Pennsylvania 19380-3428

Dear Dr. Crothall:

During an inspection of your establishment, located in West Chester, Pennsylvania, on September 2 through October 18, 2004, our investigator determined that your firm manufactures insulin infusion pumps. Insulin infusion pumps are medical devices as defined by section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. 321(h)].

The above-stated inspection revealed that these devices are adulterated under section 501(h) of the ACT [21 U.S.C. 351(h)], in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformance with the Current Good Manufacturing Practice (CGMP) requirements for medical devices which are set forth in the Quality System regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820. Significant deviations observed include, but are not limited to, the following:

1. Failure to adequately establish and maintain procedures for implementing corrective and preventive action, which include requirements for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential problems, as required by 21 CFR 820.100(a)(1). For example:

   a) It was revealed that your firm did not establish and maintain procedures for implementing corrective action with regard to certain user complaints of infusion pump failures. Your firm maintained that these types of failures had been investigated before, however the seventeen (17) design changes (DCN's) that were supposed to address the identified failure either did not correct the known failures or had never been implemented.

   b) Your firm's corrective and preventive action procedure, document number [redacted], does not adequately address the requirements of 21 CFR 820.100(a)(1), in that the procedure does not require the analysis of any sources of quality data.

c) Your firm's corrective and preventive action (CAPA) procedure is not sufficient to "identify existing and potential causes of nonconforming product, or other quality problems," as required by 21 CFR 820.100(a)(1). The procedure stipulates that a CAPA committee will meet at a minimum of once a month to review CAPA requests. The CAPA committee determines if a CAPA request warrants further review. If the CAPA committee determines that the request does in fact warrant further review, the CAPA is assigned to an employee and given a due date. Before implementing the employee's recommended corrective or preventive action, the CAPA committee again meets to review the recommendation in order to determine if the action is considered appropriate. Your procedure does not include any requirements for the CAPA committee to meet for special circumstances; such as, a corrective or preventive action to correct an immediate risk to health. Therefore, it is possible that a CAPA request initiated because of a health hazard would not be reviewed by the CAPA committee for a month. Additionally, the implementation of a corrective or preventive action could also be delayed for a month under this process.

d) Your firm's Complaint Handling and Recall Procedure is inadequate in that a CAPA and the associated analysis is only implemented when trends, defined within specified statistical thresholds are reached, or, when an event reportable under the Medical Device Reporting (MDR) regulation has been identified. This procedure may not capture and therefore does not address the possibility that a single complaint, that is not an MDR event, may require implementing a CAPA. Additionally, it is unclear what the rationale is for opening a CAPA when there is an increase in complaint categories and 4 month upward trends of complaints for the installed base of devices.

e) Your firm's Complaint Handling and Recall Procedure (discussed in the preceding paragraph) was not followed. When complaints of infusion pump failures you received reached higher statistical thresholds than those that the procedure identified as triggering a review, you did not conduct a review.

2. Failure to adequately establish and maintain procedures for implementing corrective and preventive action, which include requirements for verifying or validating the corrective and preventive action to ensure that such action is effective and does not adversely affect the finished device, as required by 21 CFR 820.100(a)(4). For example, your firm's corrective and preventive action procedure, document number [redacted], does not include any requirements to verify or validate that the corrective or preventive action is effective and does not adversely affect the finished device.

3. Failure to adequately establish and maintain procedures to control product that does not conform to specified requirements, as required by 21 CFR 820.90(a). For example, your firm implemented Corrective/Preventive Action Form, Action [redacted], in order to correct an out-of-specification drill point. This nonconformity caused a force sensor to lose contact with a ball bearing intermittently, which caused the insulin pump to experience

loss of prime. The corrective action taken for future production was to visually inspect the drill points to ensure a maximum drill point of .010 inches. However, your firm did not extend your corrective action to include product already in stock.

4. Failure to establish and maintain procedures for rework, to include retesting and reevaluation of the nonconforming product after rework, to ensure that the product meets its current approved specifications, as required by 21 CFR 820.90(b)(2). For example, the current inspection revealed that infusion pump s/n [redacted] was returned three times under the same complaint code for infusion pump failures. The user complaints of pump failures associated with this pump were reported from March 2004 through August 2004. After the third user complaint of infusion pump failure, this pump was again in the queue to be refurbished. We would note that in your April 14, 2004 written response to our previous inspection of your firm (February and March 2004) you promised to revise your procedures as follows, "...to prohibit the further refurbishing of a previously refurbished pump that is returned with the same complaint code."

Additionally, the above-stated inspection revealed that your devices are misbranded under section 502(t)(2) of the Act [21 U.S.C. 352(t)(2)], in that your firm failed or refused to furnish any material or information required by or under section 519 respecting the device and 21 CFR Part 803 (Medical Device Reporting (MDR) regulation). Significant deviations include, but are not limited to, the following:

1. Failure to provide all information required in 21 CFR 803.50, Manufacturer Reporting Requirements, that is reasonably known to the manufacturer, as required by 21 CFR 803.50(b). For example, your firm is not collecting the information needed to determine if the reported events meet the definition of reportable serious injuries, in that the clinical outcome and subsequent medical intervention of the patient is not asked for. Additionally, your firm failed to identify the Type of Reported Event (Block H.1) on the 3500A form for approximately 41 MDRs. Also, your firm incorrectly identified the event type on numerous MDRs as malfunction events.

2. Failure to submit an MDR within 30 days of receiving or otherwise becoming aware of information that reasonably suggests that a marketed device may have caused or contributed to a death or serious injury, as required by 21 CFR 803.50(a)(1). For example, your firm failed to submit complaint number [redacted] as a serious injury MDR within 30 days of becoming aware of the event, which involved a patient being hospitalized with diabetic ketoacidosis after the pump failed to operate as stated in the user guide. It is important to note that this event was also reported incorrectly as a malfunction instead of a serious injury, when it was finally reported.

3. Failure to submit an MDR within 30 days of receiving or otherwise becoming aware of information that reasonably suggests that a marketed device has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury, if the malfunction were to recur, as required by

21 CFR 803.50(a)(2). For example, your firm failed to submit MDR reports to the FDA within 30 days for the following complaints: [redacted]

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the close of the inspection may be symptomatic of serious underlying problems in your firm's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. You also must promptly initiate permanent corrective and preventive action on your quality system.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no applications for premarket approval of Class III devices to which the Quality System regulation deficiencies are reasonably related will be approved until the violations have been corrected. Also, no requests for Certificates to Foreign Governments will be granted until the violations related to the subject devices have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties.

Please notify this office in writing within fifteen (15) working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to prevent the recurrence of similar violations. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to William J. Forman, Compliance Officer, Food and Drug Administration, 2nd & Chestnut Streets, Room 900, Philadelphia, Pennsylvania 19106.

Sincerely yours,

Peter C. Rinder for

Thomas D. Gardine
District Director
Philadelphia District Office
Food and Drug Administration